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Adaption of cardio-respiratory balance during day-rest compared to deep sleep—An indicator for quality of life?

Dietrich von Bonin [a], Vincent Grote [b], Caroline Buri [c], Dirk Cysarz [d], Peter Heusser [d], Max Moser [b], Ursula Wolf [a], Kurt Laederach [c,*]

[a] Institute of Complementary Medicine, University of Berne, Inselspital, Imhoof-Pavillon, 3010 Berne, Switzerland
[b] Institute of Physiology, Medical University of Graz, Austria and Human Research, Institute for Health Technology and Prevention Research, Weiz, Austria
[c] Department of Endocrinology, Diabetology and Clinical Nutrition, Autonomic Lab, University Hospital Inselspital, University of Berne, Murtenstrasse 21, CH-3010 Bern, Switzerland
[d] Chair for Theory of Medicine, Integrative and Anthroposophic Medicine, Faculty of Health, University of Witten/Herdecke, Germany

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ABSTRACTS

Heart rate and breathing rate fluctuations represent interacting physiological oscillations. These interactions are commonly studied using respiratory sinus arrhythmia (RSA) of heart rate variability (HRV) or analyzing cardiorespiratory synchronization. Earlier work has focused on a third type of relationship, the temporal ratio of respiration rate and heart rate (HRR). Each method seems to reveal a specific aspect of cardiorespiratory interaction and may be suitable for assessing states of arousal and relaxation of the organism. We used HRR in a study with 87 healthy subjects to determine the ability to relax during 5 day-resting periods in comparison to deep sleep relaxation. The degree to which a person during waking state could relax was compared to somatic complaints, health-related quality of life, anxiety and depression. Our results show, that HRR is barely connected to balance (LF/HF) in HRV, but significantly correlates to the perception of general health and mental well-being as well as to depression. If relaxation, as expressed in HRR, during day-resting is near to deep sleep relaxation, the subjects felt healthier, indicated better mental well-being and less depressive moods.

1. Introduction

Beat-to-beat changes of heart rate (HR), i.e. heart rate variability (HRV), can be analyzed in the "time domain" by statistical measures (e.g. average, standard deviation) or in the "frequency domain" using spectral analysis. In the frequency domain different frequency bands have been defined (high frequency—HF, low frequency—LF, very low frequency—VLF), ultra low frequency—ULF) and it has been shown that they may be used as indicators of autonomic nervous system (ANS) activity (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). The high frequency band (HF) reflects vagal activity, whereas low frequency (LF) is an indicator of both sympathical and parasympathical influences on HR and captures baroreflex rhythm. VLF expresses vagal and renin-angiotensin system effects and ULF circadian influences on HRV (Stein and Pu, 2012).

Respiratory activity modulates cardiac action, giving rise to respiratory sinus arrhythmia (RSA). By analyzing beat-to-beat changes of the RR-interval, i.e. the RR interval series, using a single channel ECG with a sufficiently high sampling rate and without artifacts from physical activity, it is possible to obtain clinically reliable respiration frequency from RSA during resting periods. In addition, as a consequence of respiration induced diaphragm movements, changes of the electrical axis of the heart can be used to derive respiration frequency from the ECG (Cysarz et al., 2008b; Moody et al., 1986).

Heart rate and breathing rate represent two weakly coupled physiological oscillations. Analysis of this interaction has been a challenge for decades (Pessenhofer and Kenner, 1975). Recent work focused e.g. on cardio-respiratory phase synchronization. This type of coordination represents the occurrence of heartbeats at the same phase of consecutive respiration cycles and changes significantly during sleep stage transitions, but seems to be hardly correlated with RSA (Bartsch et al., 2012). Further methods to determine synchronization of the two rhythms have been used (Hamann et al., 2009; Moser et al., 1995; Schafer et al., 1998). Recently, cardiorespiratory coordination has been suggested as an indicator of general health (Cabiddu et al., 2012).

However, some recent scientific work analyzing the temporal ratio of respiration and heart rate regardless of synchronization or coordination (heart respiration ratio, HRR) has not gained

* Corresponding author. Tel.: +41 31 632 8313; fax: +41 31 632 4167.
E-mail address: kurt.laederach@dkf.unibe.ch (K. Laederach).

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much attention although this ratio is the basis for the analysis of cardiorespiratory synchronization. HRR exhibits a circadian rhythm (Bettermann et al., 2002) which varies considerably during the day in the same individual and between different individuals. HRR is particularly influenced by physical activity (Moser et al., 1995) and possesses the unique feature of approaching a median of four (4) heart beats per breathing cycle during night sleep among larger samples. This ratio seems to be independent of the individual's heart rate pattern during day and at night and even of the study population being examined (Cysarz et al., 2008a; Hildebrandt, 1999). The decrease of heart rate is primarily attributed to the change of posture from upright to the supine position during nocturnal sleep, whereas the reduction of respiration rate is mainly a consequence of the transition from waking to sleeping (Naifeh et al., 1987).

HRR can be used as a simple measure of cardio-respiratory coordination (Hoyer et al., 2004) and to assess the ability to recover after physical activity (Hildebrandt, 1999; Matthiolius et al., 1995). Even if HRV and HRR detection uses the same source of physiological information from the basic data of an ECG, HRR and all other HRV parameters barely correlate during night sleep and there is only a weak correlation of HRR and HRV observed during the day (Cysarz et al., 2008a).

Accordingly, the information contained in HRR differs from the information contained in HRV and its relationship with physiological and psychological parameters is still unsatisfactorily explained.

1.1. Heart rate variability, sleep and health

HRV shows a significant 24 h circadian variation. It has been suggested that deep sleep is an optimal condition for determining HRV (Brandenberger et al., 2005). Among all, the first deep sleep phase is usually the longest and therefore particularly suitable for investigating cardio-respiratory variables. HRV can be used to differentiate between REM sleep and NREM sleep. Heart rate decreases in association with decreased variability in sleep stages 1–4, whereas HR increases in REM sleep. HF increases in deep sleep, peaking in stages 3 and 4 (Zemaityte et al., 1984). During deep sleep, the LF/HF quotient is low and also the interbeat autocorrelation coefficient decreases (Otzenberger et al., 1998). Before and during REM sleep phases, sympathetic activity increases and likewise LF/HF (Cabiddu et al., 2012). Spectral bands in the electroencephalogram (EEG) are closely linked to cardiac autonomic activity in the LF and HF-bands of HRV. Among the EEG bands, the delta power band varies mostly in response to HF variability, reflecting vagal cardiac autonomic regulation. It has also been observed, that changes in cardiac autonomic activity precede changes in the EEG power bands during sleep (Jurysta et al., 2003). Deep sleep is characterized by long-wavelength EEG activity (Slow-Wave-Activity, SWA). SWA peaks during the first hours of sleep and diminishes evenly during a sleep cycle.

Cardio-respiratory phase-synchronization is high during deep sleep and low during REM sleep. Episodes of n:m synchronization occur in all sleep stages with a dominance of n:1 synchronization. There is a consistent decrease in synchronization observed in stage transitions from deep sleep to REM (Bartsch et al., 2007; Bartsch et al., 2012).

Cardio-respiratory phase synchronization changes in accordance with the state of health and is more pronounced in athletes than in non-athletes (Cabiddu et al., 2012). Deep sleep deprivation had a substantial effect on sleepiness, motor and cognitive performance, and mood during the following day (Ferrara et al., 1999). In conclusion, a sufficient duration of deep sleep seems to be important for physical recovery, alertness and concentration ability.

A short resting period during the day of <30 min improved alertness and learning ability. In contrast, longer resting periods have been associated with less favorable mental performance and are correlated to higher morbidity and mortality, particularly in the elderly (Dhand and Sohal, 2006). Little is known of how much the duration of a resting period influences HRR and HRV.

In an earlier study (von Bonin et al., 2001) we found indications for a correlation between the state of health and the ratio of HRR during day-resting (D-HRR) and HRR during the first deep sleep phase (NREM-HRR). This ratio D-HRR/NREM-HRR was defined as day-night-index-HRR (DNI-HRR). Thus, it might represent a persons' ability to quickly achieve a parasympathetic state during the day and could be used as an indicator for adaptation and recovery ability. In this exploratory case study, we investigated the behaviors of HRV and HRR of healthy individuals under normal life conditions in relation to physical health and well-being, using five short resting-periods during the day and the first deep sleep phase of the night for assessment.

We hypothesize that HRV and HRR contain different information. Second, a DNI-HRR close to 1 corresponds to a better state of physical health and better well-being than a DNI-HRR considerably higher than 1. The more HRR (and possibly the HRV-variables) during a day-rest corresponds to the same values during the first phase of deep sleep, the better the regenerative ability of the organism will be.

2. Methods

2.1. Study participants

All holders of a life insurance policy (in one company) of $>200{,}000$ Swiss Francs in the canton of Berne, Switzerland, born between 1954 and 1968 ($n=300$) received a postal invitation to participate in the study. Out of these, 167 persons announced interest in participating. They received a detailed description of the study, including an informed consent. On receiving written consent, a first consultation was arranged with the study physician. Of those interested ($n=167$), 140 persons fulfilled the entry criteria and were enrolled in the study. They received a second appointment at the Insel Hospital Berne for a detailed physical examination, taking of blood sample, and instructions. Final inclusion criteria were good physical health and mental well-being (see Tables 2 and 3). Exclusion criteria were heart disease, hyper- or hypotension, diabetes mellitus, obesity, smoking, menopause, as well as treatment at the time with beta-blockers, other antiarrhythmics, antibiotics and psycho-active medication and severe sleep disorders. The study was approved by the local ethics committee (KEK 21/04). No remuneration was provided to the participants.

2.2. Examination sequence

A medical intern collected a structured history, performed a physical examination and draw a blood sample of the subjects. To assess subjective somatic complaints, health-related quality of life and the most frequent mental impairments, the Freiburg List of Complaints FBL, the Short-Form-12 Health Questionnaire SF-12 and the Hospital Anxiety and Depression Scale HADS-D were applied (Laederach-Hofmann et al., 2007). The participants then received instructions and a Holter ECG was attached. The participants had to fill in an activity protocol (diary) to note activities and sleeping times during the recording. They were instructed to lie down and relax at their home or work place for 15 min at 9 a.m., 11 a.m., 1 p.m., 3 p.m., and 7 p.m. For this purpose, they were given a resting-set, containing pillow, blanket and a portable mat. On the following day, the participants returned the Holter ECG and materials and completed the study.

2.3. Calculation of HRV and HRR

HRV data were extracted from a single channel Holter ECG (Medikorder MK3, TOM-Medical, Graz, Austria). The sampling rate for obtaining the RR-tachogramm to calculate HRV was 4096 Hz. The ECG was saved at a sampling rate of 128 Hz to reduce memory consumption of the Holter recorder. Before analysis, the ECG was visually inspected for artifacts and analyzed with MATLAB Software (The Mathworks, Natick, MA, USA). HRV parameters in the time and frequency domains were calculated according to the standards of the Task Force (Anonymous, 1996). In the time domain, the standard deviation of normal-to-normal intervals (SDNN) reflects

total HRV, whereas RSA (log RSA) was calculated using the mean absolute difference between each heartbeat interval and the successive one. The parameters in the frequency domain were calculated using the Fast Fourier transformation of the re-sampled RR-interval series (sampling rate: 4 Hz). High-frequency power (HF) was defined as the power in the frequency range 0.15–0.4 Hz, low-frequency power (LF) in the range 0.04–0.15 Hz, and very-low-frequency power (VLF) < 0.04 Hz respectively. In the following, HF, LF and VLF are presented as ln(ms^2). The parameters were calculated for all consecutive 5-minute epochs of the recording.

In addition, the autocorrelation of the RR-interval series was calculated to determine NREM sleep phases (Otzenberger et al., 1997) using the following procedure. Each RR-interval was plotted against the preceding RR-interval, RR_{i+1} vs. RR_i (so-called Poincaré plot) and, subsequently, Pearson's correlation coefficient r_{RR} was calculated for this diagram. The correlation coefficient was also calculated for all consecutive 5-minute epochs of the recording. During sleep the time course of r_{RR} resembles sleep stages very closely. The lower r_{RR}, i.e. the more uncorrelated the series of successive RR-intervals, the deeper the sleep (Otzenberger et al., 1997). The epoch length was set to 5 min because shorter epoch lengths show more fluctuations and have a larger variance compared to epoch lengths of e.g. 5 minor 10 min. Fig. 1 shows an example illustrating the effect of different epoch lengths. The epoch length of 1 min (top diagram) shows the first local minimum at about 23:30 straight after the subject fell asleep according to the diary. However, the sequence of r_{RR}-values fluctuates largely and, hence, this sleep phase cannot be regarded as a stable NREM-sleep phase. Using an epoch length of 5 min (middle diagram) the r_{RR}-values slowly decrease and the local minimum is at 0:30. This effect is even more pronounced for the epoch length of 10 min (lower diagram). Longer epoch lengths act like a low pass filter on the r_{RR} series compared to the r_{RR} series obtained by the 1 min epoch length. The epoch length of 5 min is a good compromise because it permits a reasonable identification of the first stable NREM sleep phase and its temporal resolution is still feasible.

In this study, the first stable NREM sleep phase was defined as the first local minimum of r_{RR} during nighttime sleep that is followed by low values of r_{RR} for at least 10 min. The beginning of sleep was determined according to the diary and indicated by a clear increase of the average RR-interval. Note that r_{RR} is able to reflect the sleep cycles more closely than e.g. the ratio LF/HF from spectral analysis of HRV (Otzenberger et al., 1998).

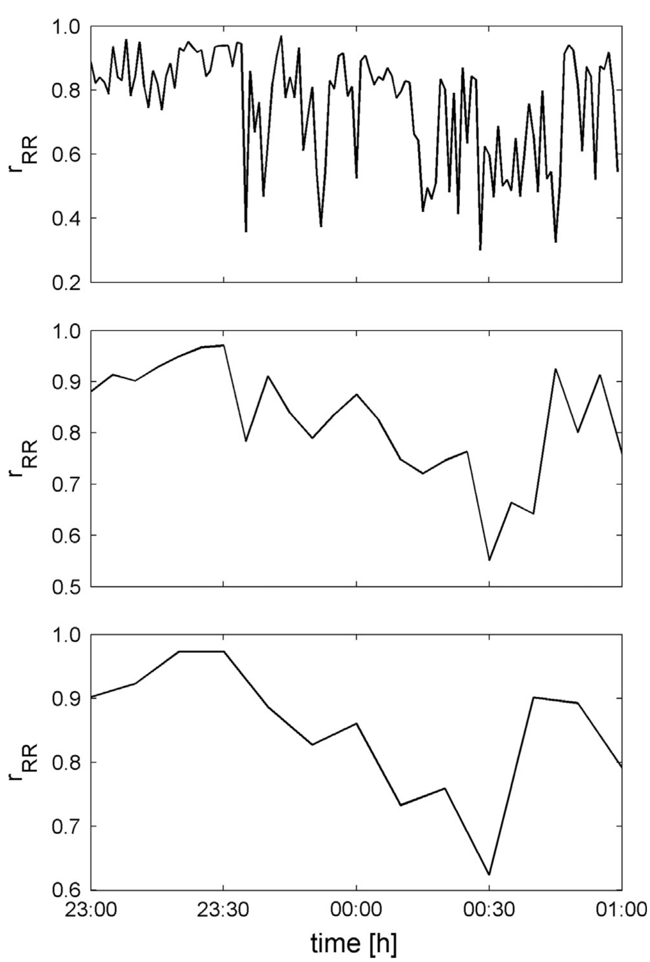

Fig. 1. Example illustrating the effect of different epoch lengths on the calcualtion of r_{RR}. The correlation coefficient r_{RR} is calculated for three different epoch lengths: 1 min (top), 5 min (middle) and 10 min (bottom). The first local minimum of r_{RR} as the first stable NREM sleep phase can only be unambigously identified using an epoch length of 5 or 10 min.

Table 1
Classification key for arrangement of study parameters.

		Tertiles		
		1	2	3
D-HRR	n	25	31	31
	range	≤ 3.77	3.78–4.23	≥ 4.24
NREM-HRR	n	30	28	29
	range	≤ 3.73	3.74–4.40	≥ 4.41
AMP-HRR	n	26	32	29
	range	≤ 0.77	0.78–1.59	≥ 1.60
		1	2	
DNI-HRR	n	40	47	
	range	≤ 1.06	> 1.06	

Captions: D-HRR: value of all resting times; NREM-HRR: HRR during first 15 min of first deep sleep phase; AMP-HRR: day/night amplitude of HRR; DNI-HRR: HRR day/night index.

The mean respiratory rate (AF) of all 5-minute epochs of the ECG was calculated using the ECG derived respiration technique (Cysarz et al., 2008b; Moody et al., 1986). HRR was determined for each of the five 15-minute resting periods during the day and the mean of all five resting periods was calculated (D-HRR). Deep sleep HRR was calculated as the mean ratio of heart rate and respiratory rate during the first deep sleep as defined above (NREM-HRR). Mean HRR was obtained also for the total duration of sleep (Sleep-HRR).The day-to-night amplitude of HRR (AMP-HRR) served as the key value for the circadian variation of HRR. The day/night-index-HRR (DNI-HRR) was defined as the ratio D-HRR/NREM-HRR.

2.4. Statistics

HRV variables, as well as the standardized psychometric scales from the questionnaires are represented as continuous variables. General linear models (GLM) were used to perform several independent univariate tests like Student's *t*-test and single factor variance analysis (ANOVA). No replacements of missing data were performed (listwise case exclusion). Calculations were performed with SPSS (IBM, La Jolla, California, USA) and MATLAB (The Mathworks, Natick, MA, USA) software. T-HRR, NREM-HRR, Sleep-HRR, AMP HRR (and DNI-HRR) are approximately normally distributed. For further statistical analysis, the first four variables were grouped into tertiles. According to the second hypothesis the (ln)DNI-HRR (+1) was dichotomized (see Table 1).

3. Results

Of the 140 participants, 127 Holter ECG were suitable for analysis. To be included in the statistical analysis, all resting periods and all questionnaires had to be completed. Because it was challenging for the participants to integrate all five resting periods into their daily routine, only 87 of the 127 data sets fulfilled all criteria to be included in the final analysis. The socio-demographic data of the study population is shown in Table 2. As expected, there are significant differences in height, weight and BMI between men ($n=48$) and women ($n=39$). There was no difference in mean age and gender. The average age of the subjects was 41.9 ± 4.3 years.

3.1. Psychometric scales

According to the questionnaires participants showed few physical and mental complaints. Most values of the psychometric scales were within the normal range for age and gender (Table 3).

There were significant associations among several dimensions/ scales of the three psychometric instruments: total complaints in the FBL correlated with SF12 somatic and mental scale: ($r=-0.47/-0.44$) and with HADS-D anxiety and depression: $r=0.57/0.53$.

Table 2
Socio-demographic data of study sample (n=87).

	Sex	Mean	S.D.	Min	Max	$F_{(1,\ 85)}$	p
Age	*female*	41.33	4.32	35.0	49.0		
	male	42.48	4.29	36.0	50.0		
	total	41.97	4.32	35.0	50.0	1.53	0.220
Weight	*female*	60.58	8.25	47.5	79.0		
	male	78.52	7.83	62.0	100.0		
	total	70.48	12.00	47.5	100.0	107.68	0.000
Height	*female*	167.28	4.95	158.0	177.0		
	male	177.81	5.08	164.0	190.0		
	total	173.09	7.26	157.0	190.0	94.50	0.000
BMI	*female*	21.62	2.55	17.2	28.1		
	male	25.09	2.31	21.0	32.2		
	total	23.54	2.97	17.2	32.2	44.41	0.000

Captions: Age: Years; Weight: Kilograms; Height: Centimeter; BMI: Body mass index.

Table 3
Selected psychometric data of study sample (n=87).

	Sex	Mean	S.D.	Min	Max	$F_{(1,\ 85)}$	p
Somatic scale	*female*	55.04	4.39	39.5	60.7		
	male	56.70	3.15	50.2	63.3		
	total	55.96	3.82	39.5	63.3	4.08	0.047
Mental scale	*female*	52.40	5.58	38.1	59.7		
	male	52.45	6.07	33.0	60.4		
	total	52.43	5.82	33.0	60.4	0.00	0.968
Anxiety	*female*	4.43	2.73	0.0	10.0		
	male	4.11	2.74	0.0	14.0		
	total	4.24	2.72	0.0	14.0	0.28	0.599
Depression	*female*	2.06	2.00	0.0	8.0		
	male	2.51	2.17	0.0	7.0		
	total	2.32	2.10	0.0	8.0	0.94	0.336

Captions: Somatic scale: Somatic scale total score in SF 12; Mental scale: Mental scale total score in SF 12; Anxiety: Anxiety total score in HADS; Depression: Depression total score in HADS.

The mental scale-total of the SF-12 correlated with anxiety and depression in the HADS-D ($r = -0.54/-0.53$). Most associations showed gender dependence. The correlations among the variables were more pronounced in women, e.g. FBL total complaints with HADS-D anxiety and depression in men (r=0.47/0.46) in woman (r=0.59/0.75).

3.2. HRV and HRR

In Table 4, the mean values of HRR during day and night, as well as the values DNI-HRR and AMP-HRR, are depicted. It is evident that the average day-resting HRR was close to 4, i.e. on average 4 heartbeats occurred during each respiratory cycle. The first deep sleep (NREM sleep) appeared on average 40 min after the beginning of sleep as noted in the diary and was indicated by a clear increase of the average RR-interval). During this sleep epoch HRR decreased to 3.8 whereas the mean HRR during sleep was again close to 4. HRR was similar during the 5 day-time resting periods and all HRV measures and HRR strongly correlated among the 5 day-resting periods (Fisher's Z'=0.785–0.809, $p < 0.01$).

Regarding gender differences, we observed a main effect and significant interaction in the diurnal variations of LF/HF and sex (F=2.62, p=0.024). The male participants showed a marked activation of sympathetic tone in the morning resting period compared to deep sleep, which fell continuously during the day. For women, an evenly increasing activation of LF/HF balance during the day was recognized (Fig. 2)

Table 5 shows the relationships between HRR variables and HRV in waking state, sleep and during the day-resting periods.

Table 4
Heart Respiratory Rate Quotient (HRR) during day and night.

	Mean	S.D.
D-HRR (9 a.m.–7 p.m.)	**4.10**	**0.56**
9 a.m.	4.19	0.67
11 a.m.	4.08	0.63
1 p.m.	4.17	0.61
3 p.m.	4.07	0.63
7 p.m.	4.01	0.63
NREM-HRR (deep sleep)	**3.84**	**0.59**
Sleep-HRR	**4.12**	**0.74**
AMP-HRR	**1.31**	**0.85**
DNI-HRR	**1.08**	**0.13**

Captions: D-HRR: HRR mean value of all resting times; NREM-HRR: HRR during first 15 min of first deep sleep phase; Sleep-HRR: Mean HRR during all sleep phases; AMP-HRR: day/night amplitude of HRR; DNI-HRR: HRR day/night index HRR=D-HRR/NREM-HRR.

D-HRR and NREM-HRR were significantly correlated with heart rate and respiratory rate in all conditions. DNI-HRR related to respiratory rate only during sleep. Among the HRR variables, the DNI-HRR correlated significantly with D-HRR (r=0.33, $p < 0.01$), with NREM-HRR ($r = -0.51$, $p < 0.01$) and with AMP-HRR (r=0.26, $p < 0.05$).

With respect to HRV, the DNI-HRR (in contrast to T-HRR, NREM-HRR and AMP-HRR) apperared as an independent parameter of cardiorespiratory interaction analysis. No significant correlations with HRV variables were found. Noteworthy was the limited relationship of balance (LF/HF) to the different other HRR variables. Respiration is represented mainly in the HF band of HRV. However, HF only showed a weak correlation with the parameters of HRR, except DNI-HRR, even if partially significant (see Table 5). More pronounced were the relationships of VLF and TP to D-HRR during wake state and in sleep.

3.3. Psychometric data and HRR

In Table 6, significant effects of the DNI-HRR with the scales “perception of general health” and “mental well-being” in SF-12, as well as “depression” in HADS are shown. The participants showing a DNI-HRR ≤ 1.06 scored a mean of 86.15 (SD 10.93) in perception of general health, whereas the group with DNI-HRR > 1.06 scored 79.09 (SD 14.35). Regarding mental well-being, those participants with DNI-HRR ≤ 1.06 scored a mean of 81.36 (9.25), and the group with DNI-HRR > 1.06 scored 75.65 (S.D. 13.00). Similarly, depressive moods were less pronounced among those with DNI-HRR ≤ 1.06 (mean 1.83, S.D. 1.58) and higher in the group DNI-HRR > 1.06 (mean 2.79, S.D. 2.4). In conclusion, participants with a DNI-HRR < 1.06 felt healthier, indicated better mental well-being and less depressive moods. Of the other HRR values, only NREM-HRR had a significant effect on perception of general health. From the Freiburg complaints list (FBL) nervousness correlated weakly with D-HRR (F=4.17, $p < 0.05$; not illustrated).

4. Discussion

In this exploratory study, healthy subjects aged 35–50 years and holding a life insurance policy, were investigated with respect to the ratio between heart rate and respiratory rate (HRR) during wake state, day-rest and sleep. HRR is regarded as an indicator of an ergotropic, respectively a trophotropic state of the organism (Perlitz et al., 2004). Of special interest was the relationship of HRR during the day-resting periods, to HRR in deep sleep (DNI-HRR), which we examined for its capacity to express the degree to which

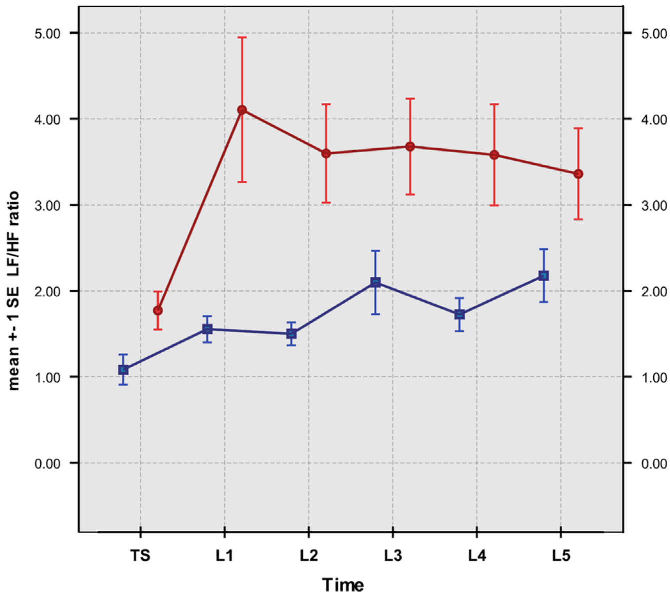

Fig. 2. Gender differences for mean LF/HF ratio. LF/HF—ratio of high frequency and low frequency according to sex. Median difference between sexes=1.659, SE=0.566; CI 95%: 0.534–2534–2.785, main effect sex: $p=0.004$ (interaction: time × sex: $p=0.024$). TS—deep sleep. L1–L5—resting times during the day. Red—male (upper line, dots). Blue—female (lower line, squares).

a subject is able to relax during day-resting. We examined the hypotheses generated in earlier studies (Cysarz et al., 2008a; von Bonin et al., 2001) where the HRR and especially the DNI-HRR included information other than heart rate variability (HRV) which, however, was related to physical and mental health.

The first part of our hypotheses was confirmed: the DNI-HRR emerged as an independent parameter compared to HRV parameters. In particular, DNI-HRR only minimally correlated with LF/HF. A more pronounced relationship would be expected because LF/HF is regarded as an indicator of the sympathico-vagal balance, as is HRR, and both are connected with activation and recovery states of the organism. Although the influence of breathing on heart rate variability is mediated by vagal tone and expressed in HF, log RSA and LF/HF, these parameters correlated only weakly with the DNI-HRR. However, there were clear indications for a correlation of the DNI-HRR with perceived health: although the study population exhibited a high level of physical and mental well-being and thus only showed a limited variance of psychometric values, the DNI-HRR was significantly correlated with mental well-being, awareness of physical health and depressive symptoms. In this context, we would expect that such a relationship will become more prominent in patients with psychiatric or medical conditions.

Following our hypothesis, only a few individuals reached a state of relaxation during the day deeper than in non-REM sleep (DNI-HRR <1). Whether this is a sign of a specific pathology cannot be inferred from our sample. Among participants with reduced ability to relax (DNI-HRR >1), the associations of DNI-HRR and psychometric values are more prominent than in others: the less a person attains the HRR of deep sleep during day-rest, the more unfavorable perceived health, mental well-being and depressive mood will be. In contrast, the information obtained from patient history and clinical examination produced no significant results (not illustrated).

In our view, the high intra-subject test-retest-reliability of all variables in the five daytime resting periods allows to only use one resting period for determining the day-rest HRR variables in future studies. This parameter is easily derived from a routine recording

Table 5
ANOVA-F statistics and significance-levels for HRR with HRV-variables during day-resting, sleeping and waking state.

		D-HRR $F_{(2,\ 84)}$		NREM-HRR $F_{(2,\ 84)}$		AMP-HRR $F_{(2,\ 84)}$		DNI-HRR $F_{(1,\ 85)}$	
Supine	HR	75.71***	+	19.23***	+	5.51**	+	1.65	
	AF	6.21***	–	4.65*	–	1.37		0.03	
	LF/HF	0.86		0.65		0.05		0.93	
Sleep	AF	2.63		27.32***	–	0.44		3.88*	+
	HR	40.41***	+	25.88***	+	0.64		0.02	
	HF	3.42*	–	1.69		2.27		0.01	
	LF	7.84**	–	2.83		6.04**	~	0.01	
	TP	11.14***	–	4.29*	–	5.89**	~	0.06	
	VLF	16.34***	–	6.53**	–	5.87**	~	0.29	
	log RSA	9.82***	–	8.96***	–	3.10		0.01	
	SDNN	12.63***	–	6.27**	–	5.83**	~	0.05	
	LF/HF	3.34**	~	0.08		0.28		0.08	
Awake	AF	3.64*	–	11.03***	–	19.41***	–	0.11	
	HR	41.38***	+	16.80***	+	6.29**	+	0.42	
	HF	4.63*	–	3.25*	–	6.13**	~	0.12	
	LF	5.07**	–	1.62		10.08***	~	0.04	
	TP	14.04***	–	6.08**	–	7.94**	~	0.01	
	VLF	19.84***	–	8.55	–	7.23**	~	0.00	
	log RSA	15.38***	–	12.43****	–	10.17***	~	0.05	
	SDNN	16.58***	–	7.06**	–	7.58**	~	0.09	
	LF/HF	1.58		2.05		7.34**	+	0.10	

Captions: D-HRR: HRR mean value of all resting times; NREM-HRR: HRR during first 15 min of first deep sleep phase; AMP-HRR: day/night amplitude of HRR; DNI-HRR: HRR day/night index HRR=D-HRR/NREM-HRR; AF: Respiratory rate; HR: Heart rate; HF: High frequency-HRV; LF: Low frequency-HRV; TP: Total Power-HRV; VLF: Very low frequency-HRV; log RSA: Respiratory sinus arrhythmia; SDNN: Standard deviation of RR-intervals; LF/HF: Quotient of Low Frequency-HRV/High Frequency-HRV; +: The HRV variable increases in the group obtained by HRR classification from 1 to 3 (2); ~: The HRV variable shows a non-linear trend in the group obtained by HRR classification from 1 to 3 (2); –: The HRV variable decreases in the group obtained by HRR classification from 1 to 3 (2).

* $p < 0.05$
** $p < 0.01$
*** $p < 0.001$

of a Holter ECG with appropriate software to calculate the respiratory rate. In considering the circadian position and duration of the resting period, there is evidence for a start around 3 p.m. and a duration of 10 – 45 min to optimally contribute to recovery and mood elevation (Dhand and Sohal, 2006). Patients with major depression (MD) benefited in subjective well-being from a day-time rest of about 50 min between 2 and 3 p.m. (Peth et al., 2012). On the other hand, a resting period in the morning after sleep deprivation produced unpleasant mood changes compared to an afternoon sleep in such patients. Furthermore, neither the amount of deep sleep nor REM-sleep seemed to have any direct influence on mood changes (Wiegand et al., 1993). MD patients showed significantly lower REM-latencies during day-napping but no difference in REM-density compared to control persons (Peth et al., 2012). In healthy subjects, the amount of REM-sleep determined the positive effect of an afternoon nap on emotional stability. Hence, the progressive responsiveness during the day to anger and fear of others was eliminated by an afternoon rest and the ratings of positive emotions enhanced (Gujar et al., 2011).

As depressive mood in our study is correlated with an elevated DNI-HRR, we propose to investigate, whether the limited cardio-respiratory recovery ability in people with depressive moods could be improved—as expressed in DNI-HRR reduction—by a short afternoon sleep. The sensitivity of the DNI-HRR to depression in our study is not self-understood, as the degree of depression only has a weak influence on autonomic modulation of HRV and blood pressure variability (BPV) (Rottenberg, 2007). Even the non-linear parameters of HRV and BPV showed no correlation to the severity

Table 6
HRR relationships (ANOVA-F statistics) with selected items of questionnaires SF-12 and HADS-D.

		D-HRR $F_{(2,\ 84)}$	NREM-HRR $F_{(2,\ 84)}$	AMP-HRR $F_{(2,\ 84)}$	DNI-HRR $F_{(1,\ 85)}$
SF-12	**Somatic scale total**	0.90	0.09	0.20	0.54
	Mental scale total	0.97	2.16	0.08	2.21
	Functional physical ability	0.66	0.58	1.24	0.06
	Physical role function	0.11	0.70	1.77	0.07
	Somatic pains	2.29	0.85	0.60	0.38
	Perception of general health	0.50	**3.34***+	0.10	**6.33***−
	Alertness	1.09	0.60	0.35	0.36
	Social function ability	0.91	0.80	0.21	1.95
	Emotional role function	2.23	2.77	0.82	0.31
	Mental well-being	0.67	1.13	0.02	**5.25***−
	Change in health	0.28	0.53	1.85	0.19
HADS	**Anxiety**	0.06	0.88	0.10	0.39
	Depression	0.04	1.31	0.16	**4.49***+

Captions: D-HRR: HRR mean value of all resting times; NREM-HRR: HRR during first 15 min of first deep sleep phase; AMP-HRR: day/night amplitude of HRR; DNI-HRR: HRR day/night index; SF-12Short-Form-12 Health Questionnaire HADS-D: Hospital Anxiety and Depression Scale;

+ The psychometric variable increases in the group obtained by HRR classification from 1 to 3 (2)

− The psychometric variable decreases in the group obtained by HRR classification from 1 to 3 (2)

* $p=0.05$

of the illness (Voss et al., 2011). In contrast to non-linear parameters, the HRR as the simple temporal ratio of two independent but weakly coupled physiological oscillations in the human organism, is compellingly straight forward in derivation, calculation and understanding. In earlier investigations, the HRR served also as a continuous parameter for recovery during therapy. There, HRR was usually determined by a simple method based on direct clinical observation (Hildebrandt et al., 1998). A "normalization" i.e. a trend towards the quotient of 4 from the initial HRR value was shown during therapy. If the DNI-HRR presented here will also be suitable for monitoring therapy has to be investigated.

4.1. Limitations

In interpreting the study results, several limitations need to be considered. The sampling procedure was realized by sending a letter of invitation to holders of a life insurance policy with a payout of more than 200,000 Swiss Francs in the region of the Swiss capital, Berne. Thus, the sample was taken from a high-income population with a high proportion of freelance workers at an age of increased professional pressure, which, therefore, cannot be regarded representative.

Furthermore, the individuals within this population might be more health-conscious than an average population group: this is visible in the values of all psychometric scales, the majority being in the normal range or better (HADS-D depression 15% below healthy controls). The good state of health in our population is confirmed further by the limited number of pathological findings in the clinical examinations. Interestingly, for a mainly self-employed population with a high income, the participants only noted a moderate average working time (mean 43 h/week, SD18.2). In addition, the direction of influence between the DNI-HRR and subjective health impairment cannot be inferred from the data of a correlational study. However, the well-known modulation of heart rate by emotions via the sympathetic system as well as the pronounced changes in respiratory amplitude and rate caused by stress (Ohsuga et al., 2001), provide fair clues for a causal influence of depression, perceived health and mental well-being on DNI-HRR.

In this study, the first stable NREM sleep phase (deep sleep) was determined by quantifying RR-interval dynamics (r_{RR}) as a surrogate for polysomnographic recordings. The temporal resolution to detect this sleep phase was 5 min instead of 30 s as in polysomnograpy. However, in this study the epoch duration of 5 min is advantageous because it acted like a low pass filter on fluctuations of r_{RR} occurring at epochs of shorter duration (e.g. 30 s or 1 min). Hence, the local minimum of r_{RR} using 5-minute epochs represents a stable NREM sleep phase in the sense that preceding and following 5-minute epochs also show low values of r_{RR}. NREM sleep phases could have been also detected using spectral parameters of HRV because ultradian oscillations in delta wave activity of EEG and spectral parameters of HRV are inversely coupled during sleep (Brandenberger et al., 2001). However, this coupling occurs only on average whereas in the individual recording the link between r_{RR} and sleep phases is closer (Otzenberger et al., 1998).

The size and characteristics of the sample examined make it available as a comparative group in good health with average mental and physical characteristics in the upper normal range. The conclusions regarding DNI-HRR, mental health and well-being will have to be confirmed in future studies with patients suffering psychiatric and medical conditions.

Conflict of interest

None for all authors.

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